

Serial No. 10/076,514

VÖLKE et al.

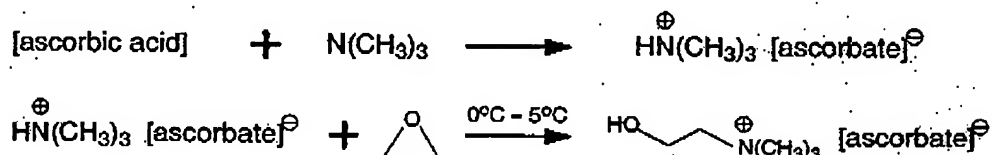
PF 0000052203

More specifically, applicants have corrected Claims 6, 12, 13 and 23 to refer to --trimethylamine-- instead of "triethylamine",<sup>2)</sup> and have revised the temperature range referenced in Claims 6 and 23 to read on "from 0°C to 5°C".<sup>3)</sup> Claim 7 was combined with Claim 6, and the solvent was further specified corresponding to the provisions set forth in Claim 23. Additionally, applicants have effected some editorial changes to allow an easier understanding of the claimed subject matter. No new matter has been added.

The Examiner rejected Claims 6, 12, 13 and 23 to 25 under 35 U.S.C. §112, ¶2, as being indefinite.

The Examiner argued in this context that the claims were unclear with regard to the requirement for diffraction lines at  $d = 3.80 \text{ \AA}$  and  $4.55 \text{ \AA}$  adding "however, the most intense lines are presumably at 3.40 and 4.70 Angstroms, far outside of the diffraction lines." It is respectfully submitted that applicants refer, firstly, to specific diffraction lines at certain distances and, secondly, to a distance range in which the most intense diffraction lines are found. To better bring out that the two requirements are separate, applicants have reworded Claim 23 to recite the phrase "... having diffraction lines at  $d = 3.80 \text{ \AA}$  and  $4.55 \text{ \AA}$ , and having diffraction lines which are most intense in a range between 3.40 and 4.70  $\text{\AA}$ , in a 2  $\Theta$ X-ray powder diffractogram ...". Favorable reconsideration of the Examiner's respective position is therefore respectfully solicited.

The Examiner further argued that Claim 23 was lacking essential steps in that "choline is never added to the mixture of ascorbic acid, solvent and water." Applicants' process can e.g. be illustrated by the following reaction scheme:



The scheme illustrates that choline does not need to be added. Rather, the choline cation is formed when the trimethylammonium cation reacts with ethylene oxide. The test of definiteness is whether a person of ordinary skill in the art would understand the bounds of the claim when reading it in the light of the supporting specification,<sup>4)</sup> and, as explained by the Board in *Ex parte Wu*<sup>5)</sup>

*In rejecting a claim under the second paragraph of 35 U.S.C. 112, it is incumbent on the examiner to establish that one of ordinary skill in the pertinent art, when reading the claims in*

2) Cf. e.g. page 2, indicated lines 39 to 43, of the application.

3) Cf. e.g. page 4, indicated lines 25 to 30, page 4, indicated line 45, to page 5, indicated line 3, and page 5, indicated lines 11 to 17, of the application.

4) Cf. *Morton Int. Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 28 USPQ2d 1190 (Fed. Cir. 1993); *Orthokinetics Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1 USPQ2d 1081 (Fed. Cir. 1986).

5) 10 USPQ2d 2031 at 2033 (BPAI 1989).

060808

- 2 -

BEST AVAILABLE COPY

**Serial No. 10/076,514**

VÖLKELE et al.

PF 0000052203

light of the supporting specification, would not have been able to ascertain with reasonable degree of precision and particularity the particular area set out and circumscribed by the claims.

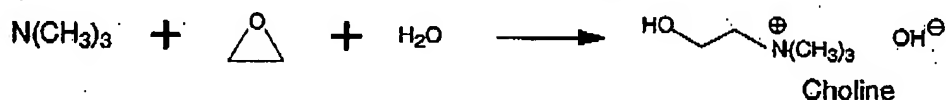
The Examiner's criticism that the claim lacked definiteness because choline was not added as a starting material in accordance with applicants' procedure is, in light of the foregoing, not deemed to establish that a person of ordinary skill in the pertinent art would not have been able to ascertain the metes and bounds of applicants' claim. It is therefore respectfully requested that the respective rejection be withdrawn.

Applicants' claims are, in light of the foregoing and the attached, deemed to be in full compliance with the provisions of Section 112, ¶2. Favorable action is solicited.

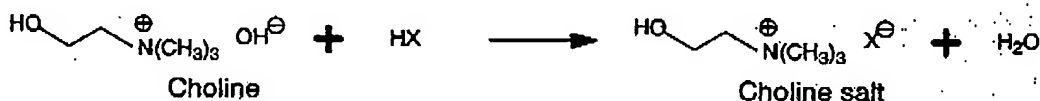
Further, the Examiner rejected Claims 6, 12, 13 and 23 to 25 under 35 U.S.C. §103(a) as being unpatentable in light of the teaching of *Klein et al.* (US 2,870,198) and *Spires* (US 4,394,377).

It is firstly noted that *Spires et al.* refer to *Klein et al.* where the synthesis of choline tartrate is concerned. However, where the synthesis of choline ascorbate is concerned *Spires et al.* refer to the disclosure of *Hoffmann* (US 2,823,166).

The teaching of *Klein et al.* provides of a general procedure for the manufacture of crystalline anhydrous salts of choline in which, in a first step, one mole of ethylene oxide is reacted with one mole of trimethylamine in an aqueous alcoholic solution (e.g. methanol) containing one mol of water per mol of said trimethylamine, as illustrated in the following reaction scheme:



The choline which is obtained in the first step is subsequently, in the reaction mixture in which it is obtained, combined with at least one mol of an acid (HX) per mol of choline and thereby forms a choline salt:



As a final measure, the choline salt is crystallized out of the reaction mixture and the crystalline anhydrous choline salt is recovered. Notably, *Klein et al.* illustrate the procedure with experiments in which choline salts of citric acid and tartaric acid are prepared, and although it is stated that the procedure can be used to produce any desired salt of choline, the use of ascorbic acid is not mentioned in the reference.

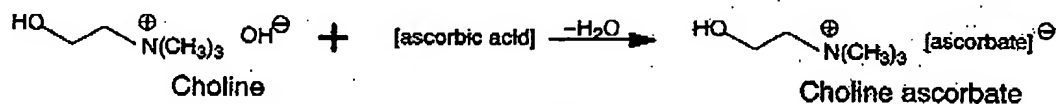
BEST AVAILABLE COPY

Serial No. 10/076,514

VÖLKEL et al.

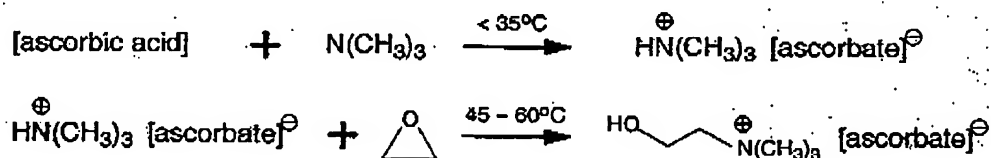
PF 0000052203

It is immediately apparent from the reaction schemes set forth in the foregoing that applicants' process differs from the procedure of *Klein et al.* because applicants' process avoids the preparation of choline itself. Moreover, and equally pertinently, the teaching of *Klein et al.* neither suggests nor implies that choline ascorbate which is prepared by the requisite procedure is crystalline. It is deemed to be of particular importance in this regard to take into account that *Spires* specifically reference the disclosure of *Hoffmann* where the ascorbate of choline is concerned. Accordingly, it is deemed essential to duly consider the particular and expressed teachings of *Hoffmann*. *Hoffmann* describes in example 1 the synthesis of choline ascorbate, and the measures which are taken by *Hoffmann* are almost identical to the synthetic steps of *Klein et al.*'s procedure: Freshly prepared choline is dissolved in methanol and subsequently ascorbic acid is added to the solution of the choline base.



The resulting choline ascorbate is isolated after treatment with carbon and after removal of the solvent. Notably, *Hoffmann* describes that the choline ascorbate which was obtained in this manner is in form of a heavy viscous oil. Considering that the measures which are taken by *Hoffmann* in the manufacture of choline ascorbate are almost identical to the steps taught by *Klein et al.*, *Hoffmann*'s disclosure corroborates that choline ascorbate which is obtained in accordance with *Klein et al.*'s procedure would reasonably be expected to be in form of a heavy viscous oil.

*Hoffmann* also describes, in example 2, a procedure in which ascorbic acid is initially reacted with trimethylamine and the resulting product is subsequently reacted with ethylene oxide:



The choline ascorbate which is recovered by *Hoffmann* under these reaction conditions is, again, described as a heavy viscous oil.

The respective procedure of *Hoffmann* differs from applicants' procedure on the one hand in the pertinent temperature of the formation of the choline salt and, on the other hand, in the consistency of the product.

Turning back to the teaching of *Klein et al.* the Examiner will note that applicants' process differs equally considerably from the prior art procedure in the temperature at which the choline salt is formed. *Klein et al.* state that it is preferred to employ a relatively concentrated alcoholic solution

Serial No. 10/076,514

VÖLKEL et al.

PF 0000052203

and further recommend that the alcoholic solution be heated or be near its reflux temperature.<sup>6)</sup> Correspondingly, the illustrative examples describe that the second step of *Klein et al.*'s procedure is conducted by adding the reaction mixture which is obtained in the first step to a refluxing alcohol solution.<sup>7)</sup> Applicants' process therefore differs from the procedure of *Klein et al.*, on the one hand, in the manner in which the starting materials are reacted with one another, and on the other hand, in the reaction conditions which are employed. Furthermore, applicants' process yields choline ascorbate in crystalline form, ie. a result which cannot reasonably be expected based on the teaching of *Klein et al.* when the disclosure of *Hoffmann* is given due consideration.

As explained in MPEP §2143, three basic criteria have to be met in order to establish a *prima facie* case of obviousness:

- (1) There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings,
- (2) there must be a reasonable expectation of success, and
- (3) the prior art reference or the combined references must teach or suggest all of the claim limitations.

Additionally, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and cannot be based on the applicant's disclosure.<sup>8)</sup> At least two of those basic criteria for establishing a *prima facie* case under Section 103(a) are not met where applicants' invention and the teachings of *Spires* and of *Klein et al.* are concerned. *Klein et al.* fails to teach or suggest all of the elements of applicants' process and also fails to provide for the necessary suggestion or motivation to do what applicants have done. *Spires* merely mention salts of choline and refers, with regard to the manufacture of choline tartrate, to the procedure of *Klein et al.*, and with regard to the manufacture of choline ascorbate, to *Hoffmann*'s disclosure. The teaching of *Spires* can therefore not be deemed to add to the information pertaining to the elements recited in applicants' claims. Nor can the teaching of *Spires* contribute to the suggestion or motivation to modify the procedure of *Klein et al.*

It is therefore respectfully urged that the teachings of *Klein et al.* and *Spires* cannot be deemed to render the subject matter of the claims which are herewith presented by applicants obvious within the meaning of Section 103(a). Favorable reconsideration of the Examiner's position and withdrawal of the respective rejection is therefore respectfully solicited.

6) Cf. col. 3, indicated line 12 et seq., of US 2,870,195.

7) Cf. e.g. col. 3, indicated lines 52 to 55, and col. 4, indicated lines 7 to 9 and 27 to 29, of US 2,870,195.

8) *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

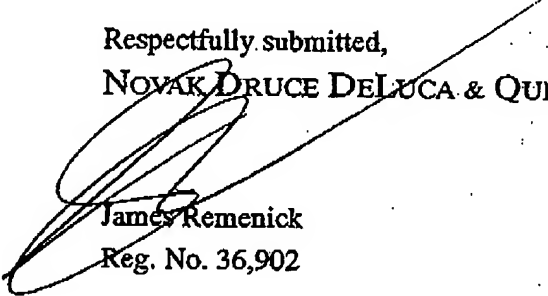
Serial No. 10/076,514

VÖLKEL et al.

PF 0000052203

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees, to Deposit Account No. 14.1437. Please credit any excess fees to such deposit account.

Respectfully submitted,  
NOVAK DRUCE DELUCA & QUIGG

  
James Remenick  
Reg. No. 36,902

1300 Eye Street, N.W.  
Suite 400 East Tower  
Washington, D.C. 20005  
(202) 659-0100

Encl.: CLAIM AMENDMENTS (Appendix I)

JR/BAS

BEST AVAILABLE COPY

060808

- 6 -